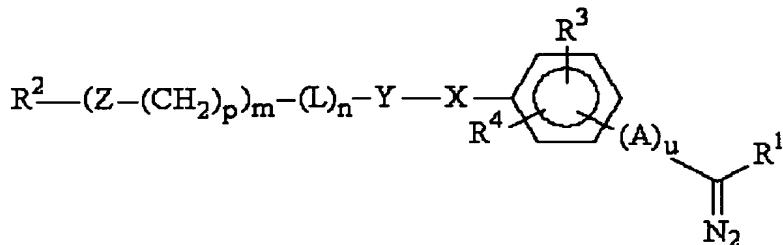


Amendments to the Claims:

The following listing of claims will replace all prior versions, and listings, of claims in the application:

1–25. (Canceled)

26. (New) A temperature-stable labeling reagent of formula (0):



in which:

R^1 represents H or an alkyl, aryl or substituted aryl group,

R^2 represents a detectable marker or at least two detectable markers interlinked by at least one multimeric structure,

L is a linker arm comprising a linear chain of at least two covalent bonds and n is an integer equal to 0 or 1,

R^3 and R^4 represent, independently of one another: H, NO_2 , Cl, Br, F, I, $R^2 - (L)_n - Y - X -$, OR, SR, NR_2 , R, $NHCOR$, $CONHR$, $COOR$, $-CO-NH-(CH_2)_3-(O-CH_2-CH_2)_3-$ CH_2-NH-R^2 , or $-CO-NH-(CH_2)_3-(O-CH_2-CH_2)_4-CH_2-NH-R^2$ with R = alkyl or aryl,

A is a linker arm comprising at least one covalent double bond enabling the conjugation of the diazo function with the aromatic ring and u is an integer between 0 and 2,

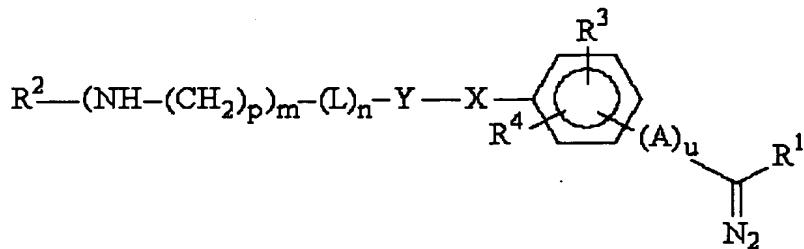
$-Y-X-$ represents $-CONH-$, $-NHCO-$, $-CH_2O-$, or $-CH_2S-$,

$-Z-$ represents $-NH-$, $-NHCO-$, $-CONH-$ or $-O-$,

m is an integer between 1 and 10, and

p is an integer between 1 and 10.

27. (New) The labeling reagent according to claim 26, of formula (1):



in which:

R^1 represents H or an alkyl, aryl or substituted aryl group,

R^2 represents a detectable label or at least two detectable labels interlinked by at least one multimeric structure,

L is a linker arm comprising a linear chain of at least two covalent bonds and n is an integer equal to 0 or 1,

R^3 and R^4 represent, independently of one another: H, NO_2 , Cl, Br, F, I, R^2 - $(L)_n-Y-X$, OR, SR, NR_2 , R, $NHCOR$, $CONHR$, $COOR$, $-CO-NH-(CH_2)_3-(O-CH_2-CH_2)_3-CH_2-NH-R^2$, or $-CO-NH-(CH_2)_3-(O-CH_2-CH_2)_4-CH_2-NH-R^2$ with R = alkyl or aryl, and

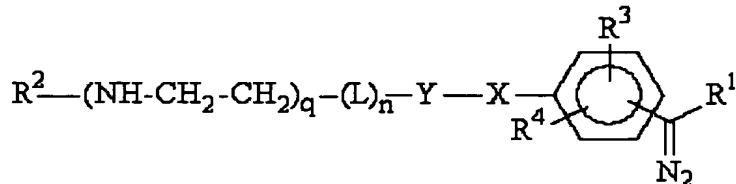
$-Y-X-$ represents $-CONH-$, $-NHCO-$, $-CH_2O-$, or $-CH_2S-$,

m is an integer between 1 and 10, and

p is an integer between 1 and 10.

28. (New) The reagent according to claim 27, wherein p is less than or equal to m .

29. (New) The reagent according to claim 27, of formula (2):



in which:

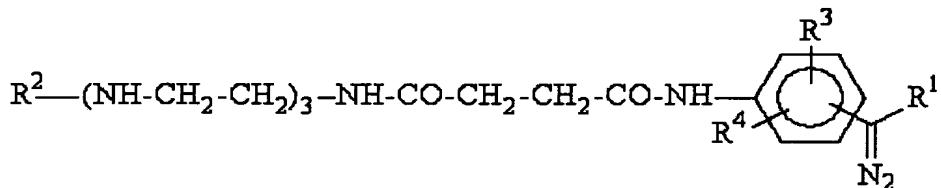
R^1 represents H or an alkyl, aryl or substituted aryl group,

R^2 represents a detectable label or at least two detectable labels interlinked by means of at least one multimeric structure,

L is a linker arm comprising a linear chain of at least two covalent bonds and n is an integer equal to 0 or 1,

R^3 and R^4 represent, independently of one another: H, NO₂, Cl, Br, F, I, R² - (L)_n-Y-X-, OR, SR, NR₂, R, NHCOR, CONHR, COOR, -CO-NH-(CH₂)₃-(O-CH₂-CH₂)₃-CH₂-NH-R², or -CO-NH-(CH₂)₃-(O-CH₂-CH₂)₄-CH₂-NH-R² with R = alkyl or aryl, and q is an integer between 1 and 10.

30. (New) The reagent, according to claim 29, of formula (3):



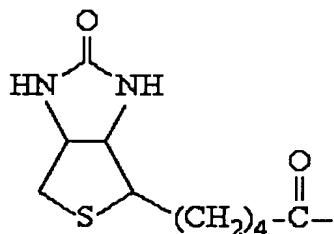
in which:

R^1 represents H or an alkyl, aryl or substituted aryl group,

R^2 represents a detectable label or at least two detectable labels interlinked by means of at least one multimeric structure,

R^3 and R^4 represent, independently of one another: H, NO₂, Cl, Br, F, I, R² - (L)_n-Y-X-, OR, SR, NR₂, R, NHCOR, CONHR, COOR, -CO-NH-(CH₂)₃-(O-CH₂-CH₂)₃-CH₂-NH-R², or -CO-NH-(CH₂)₃-(O-CH₂-CH₂)₄-CH₂-NH-R² with R = alkyl or aryl.

31. (New) The reagent according to claim 30, wherein R^2 consists of a D-biotin residue of formula (4):



32. (Withdrawn-New) The reagent according to claim 31, wherein R¹ is CH₃, and R³ and R⁴ each represent H.

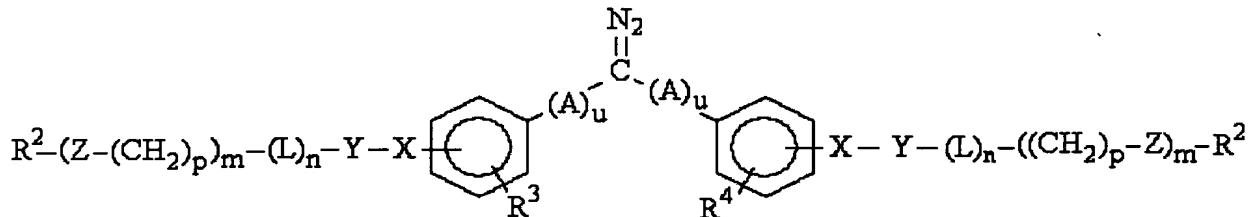
33. (Withdrawn-New) The reagent according to claim 29, in which the structure - (L)_n- consists of:

spermine or N,N'-bis(3-aminopropyl)-1,4-diaminobutane: NH₂-(CH₂)₃-NH-(CH₂)₄-NH-(CH₂)₃-NH₂, or

spermidine or N-(3-aminopropyl)-1,4-butanediamine: H₂N-(CH₂)₄-NH-(CH₂)₃-NH₂, or

a derivative containing an alanine motif: NH₂-CH₂-CH₂-COOH.

34. (Withdrawn-New) A temperature-stable labeling reagent of formula (6):



in which:

R¹ represents H or an alkyl, aryl or substituted aryl group,

R² represents a detectable label or at least two detectable labels interlinked by at least one multimeric structure,

L is a linker arm comprising a linear chain of at least two covalent bonds and n is an integer equal to 0 or 1,

R³ and R⁴ represent independently of one another: H, NO₂, Cl, Br, F, I, R² - (L)_n-Y-X-, OR, SR, NR₂, R, NHCOR, CONHR, COOR, -CO-NH-(CH₂)₃-(O-CH₂-CH₂)₃-CH₂-NH-R², or -CO-NH-(CH₂)₃-(O-CH₂-CH₂)₄-CH₂-NH-R² with R = alkyl or aryl,

A is a linker arm comprising at least one covalent double bond enabling the conjugation of the diazo function with the aromatic ring and u is an integer between 0 and 2,

-Y-X- represents -CONH-, -NHCO-, -CH₂O-, or -CH₂S-,

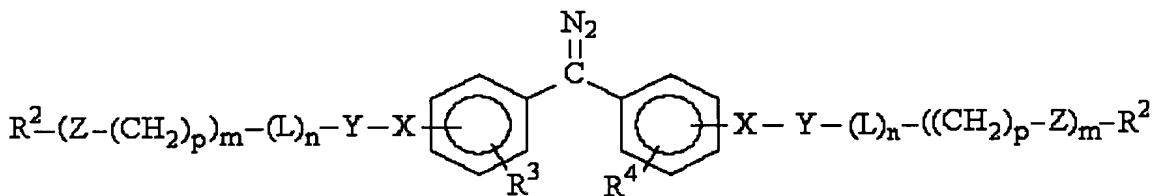
-Z- represents -NH-, -NHCO-, -CONH- or -O-,

m is an integer between 1 and 10, and

p is an integer between 1 and 10.

35. (Withdrawn-New) The labeling reagent, according to claim 34, of formula

(7):



in which:

R¹ represents H or an alkyl, aryl or substituted aryl group,

R² represents a detectable label or at least two detectable labels interlinked by at least one multimeric structure,

L is a linker arm comprising a linear chain of at least two covalent bonds and n is an integer equal to 0 or 1,

R³ and R⁴ represent, independently of one another: H, NO₂, Cl, Br, F, I, R² - (L)_n-Y-X-, OR, SR, NR₂, R, NHCOR, CONHR, COOR, -CO-NH-(CH₂)₃-(O-CH₂-CH₂)₃-CH₂-NH-R², or -CO-NH-(CH₂)₃-(O-CH₂-CH₂)₄-CH₂-NH-R² with R = alkyl or aryl,

-Y-X- represents -CONH-, -NHCO-, -CH₂O-, or -CH₂S-,

-Z- represents -NH-, -NHCO-, -CONH- or -O-,

m is an integer between 1 and 10, and

p is an integer between 1 and 10.

36. (Withdrawn-New) The reagent according to claim 26, wherein:

L comprises a motif -(O-CH₂-CH₂)-, repeated from 1 to 20 times, and

-Z- is -NH-, -NHCO- or -CONH-.

37. (Withdrawn-New) The reagent according to claim 34, wherein:

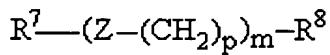
L comprises a motif -(O-CH₂-CH₂)-, repeated from 1 to 20 times, and

-Z- is -NH-, -NHCO- or -CONH-.

38. (Withdrawn-New) A method for the synthesis of a labeling reagent according to claim 26, comprising the following steps:

a) providing a label or a label precursor having a reactive function R⁶,

b) providing a linker arm of formula (8):



in which:

-Z- represents -NH-, -NHCO-, -CONH- or -O-,

m is an integer between 1 and 10,

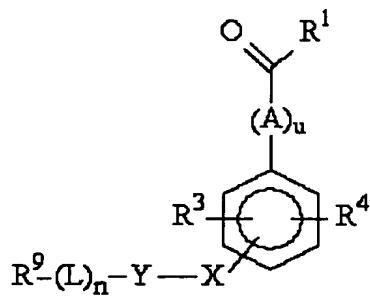
p is an integer between 1 and 10,

R⁷ and R⁸ represent two reactive functions which may be identical or

different,

c) reacting together the reactive function R⁶ of said label or label precursor and the function R⁷ of the linker arm of formula (8) in the presence of at least one coupling agent to form a covalent bond, R⁶ and R⁷ being complementary,

d) providing a derivative of formula (9):



in which:

R^1 represents H or an alkyl, aryl or substituted aryl group,

L is a linker arm comprising a linear chain of at least two covalent bonds and n is an integer equal to 0 or 1,

R^3 and R^4 represent, independently of one another: H, NO₂, Cl, Br, F, I, R²-(L)_n-Y-X-, OR, SR, NR₂, R, NHCOR, CONHR, COOR, -CO-NH-(CH₂)₃-(O-CH₂-CH₂)₃-CH₂-NH-R², or -CO-NH-(CH₂)₃-(O-CH₂-CH₂)₄-CH₂-NH-R² with R = alkyl or aryl,

-Y-X- represents -CONH-, -NHCO-, -CH₂O-, or -CH₂S-,

A is a linker arm comprising at least one covalent double bond enabling the conjugation of the diazomethyl function with the aromatic ring and u is an integer equal to 0 or 1, and

R^9 represents a reactive function complementary to R^8 ,

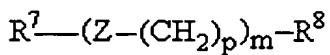
e) reacting together the reactive function R^9 of the derivative of formula (9) and the function R^8 of the linker arm of formula (8) in the presence of at least one coupling agent to form a covalent bond,

f) reacting the hydrazine or one of its derivatives with the ketone or aldehyde function to form a hydrazone, and

g) converting the hydrazone to a diazomethyl function by means of an appropriate treatment.

39. (Withdrawn-New) A method for the synthesis of a labeling reagent according to claim 34, comprising the following steps:

- a) providing a label or a label precursor having a reactive function R^6 ,
- b) providing a linker arm of formula (8):



in which:

-Z- represents -NH-, -NHCO-, -CONH- or -O-,

m is an integer between 1 and 10,

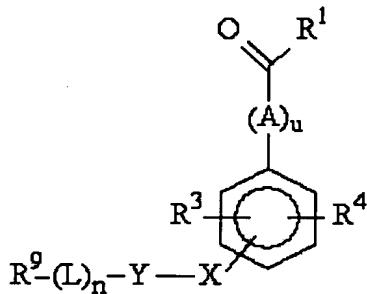
p is an integer between 1 and 10,

R⁷ and R⁸ represent two reactive functions which may be identical or

different,

c) reacting together the reactive function R⁶ of said label or label precursor and the function R⁷ of the linker arm of formula (8) in the presence of at least one coupling agent to form a covalent bond, R⁶ and R⁷ being complementary,

d) providing a derivative of formula (9):



in which:

R¹ represents H or an alkyl, aryl or substituted aryl group,

L is a linker arm comprising a linear chain of at least two covalent bonds and n is an integer equal to 0 or 1,

R³ and R⁴ represent, independently of one another: H, NO₂, Cl, Br, F, I, R²-(L)_n-Y-X-, OR, SR, NR₂, R, NHCOR, CONHR, COOR, -CO-NH-(CH₂)₃-(O-CH₂-CH₂)₃-CH₂-NH-R², or -CO-NH-(CH₂)₃-(O-CH₂-CH₂)₄-CH₂-NH-R² with R = alkyl or aryl,

-Y-X- represents -CONH-, -NHCO-, -CH₂O-, or -CH₂S-,

A is a linker arm comprising at least one covalent double bond

enabling the conjugation of the diazomethyl function with the aromatic ring and u is an integer equal to 0 or 1, and

R^9 represents a reactive function complementary to R^8 ,

e) reacting together the reactive function R^9 of the derivative of formula (9)

and the function R^8 of the linker arm of formula (8) in the presence of at least one coupling agent to form a covalent bond,

f) reacting the hydrazine or one of its derivatives with the ketone or aldehyde function to form a hydrazone, and

g) converting the hydrazone to a diazomethyl function by means of an appropriate treatment.

40. (Withdrawn-New) The method of synthesis according to claim 38, further comprising:

an additional step consisting of protection of the ketone or aldehyde function of compound (9), and

a subsequent additional step consisting of deprotection of said ketone or aldehyde function.

41. (Withdrawn-New) The method of synthesis according to claim 39, further comprising:

an additional step consisting of protection of the ketone or aldehyde function of compound (9), and

a subsequent additional step consisting of deprotection of said ketone or aldehyde function.

42. (Withdrawn-New) A method for the labeling of a biological molecule, comprising bringing into contact, in a homogeneous solution in a substantially aqueous buffer, the biological molecule and a reagent according to claim 26.

43. (Withdrawn-New) A method for the labeling of a biological molecule, comprising bringing into contact, in homogeneous solution in a substantially aqueous buffer, a biological molecule and a reagent according to claim 34.

44. (Withdrawn-New) A labeled biological molecule which can be obtained by the method according to claim 42.

45. (Withdrawn-New) A labeled biological molecule which can be obtained by the method according to claim 43.

46. (Withdrawn-New) A method for the labeling and fragmentation of a single-stranded or double-stranded nucleic acid, the method comprising:

fragmenting the nucleic acid,

attaching a label to at least one of the fragments by means of a labeling reagent chosen from the reagents according to claim 26,

said reagent coupling covalently and predominantly on at least one phosphate of said fragment.

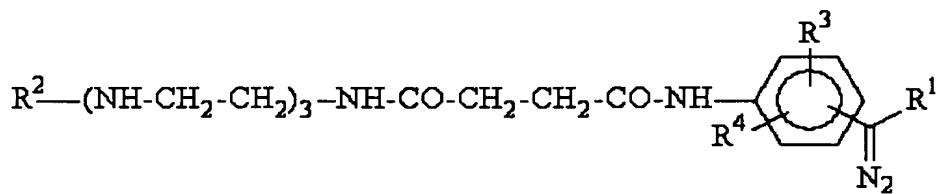
47. (Withdrawn-New) A method for the labeling and fragmentation of a single-stranded or double-stranded nucleic acid, the method comprising:

fragmenting the nucleic acid,

attaching a label to at least one of the fragments by means of a labeling reagent chosen from the reagents according to claim 34,

said reagent coupling covalently and predominantly on at least one phosphate of said fragment.

48. (Withdrawn-New) The method according to claim 46, wherein the labeling reagent is chosen from the compounds of formula (3):



in which:

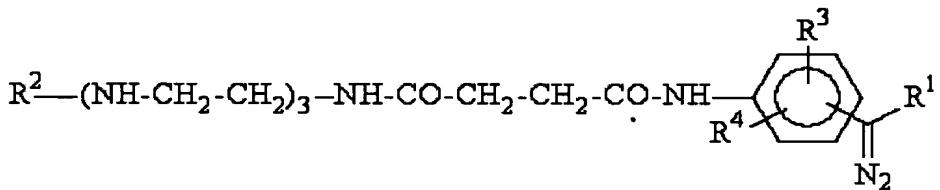
R^1 represents H or an alkyl, aryl or substituted aryl group,

R^2 represents a detectable label or at least two detectable labels interlinked by at least one multimeric structure,

L is a linker arm comprising a linear chain of at least two covalent bonds and n is an integer equal to 0 or 1, and

R^3 and R^4 represent, independently of one another: H, NO_2 , Cl, Br, F, I, R^2 - $(L)_n-Y-X-$, OR, SR, NR_2 , R, $NHCOR$, $CONHR$, $COOR$, -CO-NH-(CH_2)₃-(O- CH_2 - CH_2)₃- CH_2 -NH- R^2 , or -CO-NH-(CH_2)₃-(O- CH_2 - CH_2)₄- CH_2 -NH- R^2 with R = alkyl or aryl.

49. (Withdrawn-New) The method according to claim 47, wherein the labeling reagent is chosen from the compounds of formula (3):



in which:

R^1 represents H or an alkyl, aryl or substituted aryl group,

R^2 represents a detectable label or at least two detectable labels interlinked by at least one multimeric structure,

L is a linker arm comprising a linear chain of at least two covalent bonds and n is an integer equal to 0 or 1, and

R^3 and R^4 represent, independently of one another: H, NO₂, Cl, Br, F, I, R² - (L)_n-Y-X-, OR, SR, NR₂, R, NHCOR, CONHR, COOR, -CO-NH-(CH₂)₃-(O-CH₂-CH₂)₃-CH₂-NH-R², or -CO-NH-(CH₂)₃-(O-CH₂-CH₂)₄-CH₂-NH-R² with R = alkyl or aryl.

50. (Withdrawn-New) The method according to claim 48, wherein the fragmentation and the labeling are carried out in two steps.

51. (Withdrawn-New) The method according to claim 49, wherein the fragmentation and the labeling are carried out in two steps.

52. (Withdrawn-New) The method according to claim 48, wherein the fragmentation and the labeling are carried out in one step.

53. (Withdrawn-New) The method according to claim 49, wherein the fragmentation and the labeling are carried out in one step.

54. (Withdrawn-New) The method according to claim 50, wherein the labeling is carried out in a substantially aqueous homogeneous solution.

55. (Withdrawn-New) The method according to claim 52, wherein the labeling is carried out in a substantially aqueous homogeneous solution.

56. (Withdrawn-New) The method according to claim 51, wherein the labeling is carried out in a substantially aqueous homogeneous solution.

57. (Withdrawn-New) The method according to claim 50, wherein the fragmentation is carried out by an enzymatic, physical, or chemical process.

58. (Withdrawn-New) The method according to claim 51, wherein the fragmentation is carried out by an enzymatic, physical, or chemical process.

59. (Withdrawn-New) A labeled nucleic acid obtained by the method according to claim 46.

60. (Withdrawn-New) A labeled nucleic acid obtained by the method according to claim 47.

61. (Withdrawn-New) A kit for the detection of a target nucleic acid, comprising a labeled nucleic acid according to claim 59.

62. (Withdrawn-New) A kit for the detection of a target nucleic acid, comprising a labeled nucleic acid according to claim 60.

63. (Withdrawn-New) A solid support to which is attached a reagent according to claim 26.

64. (Withdrawn-New) A solid support to which is attached a reagent according to claim 34.

65. (Withdrawn-New) A method for the capture of nucleic acids, comprising: providing a solid support to which is directly or indirectly attached at least one biological molecule according to claim 44, the biological molecule or the nucleic acid comprising a diazomethyl function,

bringing into contact a biological sample which may contain free nucleic acids, and

washing the solid support where the molecule(s) is (are) covalently attached at least to a nucleic acid.

66. (Withdrawn-New) A method for the capture of nucleic acids, comprising the following steps:

providing a solid support to which is directly or indirectly attached at least one biological molecule according to claim 45, the biological molecule or the nucleic acid comprising a diazomethyl function,

bringing into contact a biological sample which may contain free nucleic acids, and

washing the solid support where the molecule(s) is (are) covalently attached at least to a nucleic acid.